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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/728,521	12/05/2003	Atul Varadhachary	HO-P02703US2	8270

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EXAMINER	
KAM, CHIH MIN	
ART UNIT	**PAPER NUMBER**
1656	

MAIL DATE	DELIVERY MODE
07/05/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/728,521	VARADHACHARY ET AL.	
	Examiner	Art Unit	
	Chih-Min Kam	1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 April 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,7-10,14-20,26-32 and 38-40* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,7-10,14-20,26-32 and 38-40* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *05 December 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *4/30/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of the Claims

1. Claims 1, 7-10, 14-20, 26-32 and 38-40 are pending.

Applicants' response filed April 30, 2007 is acknowledged. Applicant's response has been fully considered. Therefore, claims 1, 7-10, 14-20, 26-32 and 38-40 are examined.

Maintained Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

2. Previous rejection of claims 1, 7, 14, 17-19, 26-32 and 38-40 under 35 U.S.C. 103(a) as being unpatentable over by Van Bree *et al.* (WO 01/72322, October 4, 2001) is maintained, and the response to argument is shown below.

provisionally rejected under the judicially created doctrine of obviousness-type double patenting teach human lactoferrin (hLF) can block free LPS and cause them to clear from the body more rapidly, and mask their inflammatory activity; and hLF or LF variants (e.g., N-terminal variants with 1-4 arginine deleted, hLF-2N, hLF-3N, hLF-4N, hLF-5N; pages 4, 5 and 27), which have the biological activities of natural LF (e.g., effective in killing viruses or bacteria), can be used to treat large scale (bacterial) infection, blood-borne infection (sepsis) as well as inflammation resulting from an infection by parenteral or oral administration (pages 3-4; page 20, lines 24-29; pages 24, 26; claim 1), where the concentration of the polypeptide (LF or LF variant) in the pharmaceutical composition can be at least 1% to 20% by weight (page 24,

lines 10-12); and lactoferrin/variant can be administered orally in the form of a solid or solution, and the active components can be encapsulated in gelatin capsules together with inactive ingredients and carriers such as glucose, mannitol or magnesium carbonate (an antacid; claim 14), and the formulated solid or liquid formulations can be in an enteric-coated form (page 26; claims 7, 17-19). Although the reference does not provide a specific example for a method of treating bacteremia, enhancing a mucosal immune response or decreasing mortality using a lactoferrin composition containing the N-terminal variant, it indicates a high dose of hLF or LF variant (e.g., N-terminal variant) having the biological activity of natural LF can be orally administered, optionally in conjunction with parenteral administration because the oral administration has advantages such that the LF can be used in a matrix without little or no purification for human consumption when the LF/variant is produced by expression in a transgenic animal (page 26, lines 1-21). Van Bree teaches a method of treating large scale (bacterial) infection, blood-borne infection (sepsis) as well as inflammation resulting from an infection (see above) by parenteral and/oral administration of LF/variants to subjects, which has the same method step as the claimed invention, thus at the time of invention was made, it would have been obvious to one of ordinary skill in the art to orally administer N-terminal variant of LF in the method of treating bacteremia or sepsis, enhancing a mucosal immune response or decreasing mortality to produce the desired effect as the LF (claims 26-32, 38-40), which results in the claimed invention and was, as a whole, prima facie obvious at the time the claimed invention was made.

Response to Arguments

Applicant indicates to establish a prima facie case for obviousness, all claim limitations must be found or suggested in the references cited or within the general knowledge in the art. From Examiner's analysis, it is clear the Examiner has equated the claim term "sepsis" with any bacterial infection. Consequently, the Examiner has cited the teaching of Van Bree regarding oral Lactoferrin therapy for digestive tract infections as a pertinent disclosure. Applicant's Specification clearly defines bacteremia (paragraph [0032]) and sepsis (paragraph [0050]). The terms and the claimed methods do not encompass the digestive tract infections referred to in Van Bree as amendable to oral lactoferrin treatments. Van Bree teaches oral formulations of lactoferrin (Pg. 26-27), however, Van Bree also teaches that the "particular form of the composition varies with the intended mode of administration and therapeutic application." There is no suggestion or teaching to use oral lactoferrin in the treatment of bacteremia [0032] or sepsis [0050]. On the contrary, Van Bree teaches intravenous administration of lactoferrin at high dosages for bacteremia (Pg. 3; Examples; Pg. 22 lines 7-12). This intravenous administration is used to introduce Lactoferrin systemically to directly bind and thereby neutralize and accelerate clearance of LPS. Therefore, applicants request the rejection be withdrawn (pages 2-4 of the response).

Applicants' response has been considered, however, the argument is not found persuasive because of the following reasons. While Van Bree teaches intravenous administration of lactoferrin at high dosages for bacteremia or sepsis, the reference also indicates that oral administration of the active ingredient, optionally in conjunction with parenteral administration can be used in the treatment, and further asserts that the oral administration has advantages such

as the LF can be used in a matrix without little or no purification for human consumption when the LF/variant is produced by expression in a transgenic animal and (page 26, lines 1-21). Thus, the reference suggests oral and/or parenteral administration of the LF/variants in the treatment of bacterial infection or sepsis, and which was, as a whole, prima facie obvious at the time the claimed invention was made.

Maintained Claim Rejections-Obviousness Type Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

3. Claims 1, 7, 14, 17-19, 26-32 and 38-40 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 16-22, 26-30 and 50-51 of copending Application No. 10/663,258 (based on the amended claims filed September 26, 2006). Although the conflicting claims are not identical, they are not patentably distinct from each other because claims 1, 7, 14, 17-19, 26-32 and 38-40 disclose a method of treating bacteremia or sepsis, enhancing a mucosal response in the gastrointestinal tract or decreasing mortality of a subject having bacteremia, comprising the step of administering orally to a subject an effective amount of a lactoferrin composition comprising at least 1% to at least 50% w/w of an N-terminal lactoferrin variant to provide an improvement in the bacteremia of

said subject, wherein the N-terminal lactoferrin variant has a deletion, substitution, or combination thereof, of from 1 to 16 N-terminal amino acid residues and wherein the N-terminal lactoferrin variant retains the same biological function as full length lactoferrin; and the specification indicates sepsis or bacteremia may originate anywhere in the body such as surgical wounds or decubitus ulcers (paragraphs [0003] and [0082]). This is an obvious variation in view of claims 16-22, 26-30 and 50-51 in the copending application which disclose a method of treating a wound other than ophthalmic wounds, or enhancing the local or systemic immune system in a subject suffering from a wound by administering to the subject an effective amount of a lactoferrin composition, and the specification indicates a lactoferrin composition can have an N-terminal lactoferrin variant such as N-terminal glycine deleted or substituted or a deletion, substitution, or combination thereof, of from 1 to 16 N-terminal amino acid residues and the N-terminal lactoferrin variant retains the same biological function as full length lactoferrin (paragraphs [0009] and [0048]); and the lactoferrin composition can decrease bacterial infection of the wound (paragraphs [0102]). Both the claims of instant application and the claims of the copending application are directed to a method of treating bacteremia or sepsis, or treating wounds such as wounds causing bacteremia or sepsis by administering a lactoferrin composition comprising an N-terminal lactoferrin variant. Thus, claims 1, 7, 14, 17-19, 26-32 and 38-40 in present application and claims 16-22, 26-30 and 50-51 in the copending application are obvious variations of a method of treating bacteremia or sepsis, or wounds causing bacteremia or sepsis by administering a lactoferrin composition comprising an N-terminal lactoferrin variant.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Response to Arguments

Applicants have acknowledged the provisional double-patenting rejections and, further indicate that they are not required to address the merits of the provisional double-patenting rejections until such time as the co-pending application(s) issue and the rejections are made non-provisional (pages 4-6 of the response).

Applicants' response has been considered, since there are other rejections in this Office Action, the provisional double-patenting rejection is maintained.

Conclusion

4. No claims are allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Chih-Min Kam whose telephone number is (571) 272-0948. The examiner can normally be reached on 8.00-4:30, Mon-Fri.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Kathleen Bragdon can be reached at 571-272-0931. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Chih-Min Kam, Ph. D.
Primary Patent Examiner

CHIH-MIN KAM
PRIMARY EXAMINER

CMK
June 30, 2007